

What is Colony Collapse Disorder?

Since 2006, farmed honey bees have been disappearing yearly at an alarming rate, with losses between 30-90% of managed colonies reported by beekeepers (US Department of Agriculture). In many incidences, a hive would be depleted of adult worker bees with only the queen and a few nurse bees present to care for the immature bees (brood) in a non-functioning colony. This condition has been termed as the Honeybee Colony Collapse Disorder (or CCD). The mechanisms by which CCD occurs remains uncertain. Research evidences have implicated that a multitude of factors, such as viral pathogens, parasites, and pesticides, may contribute to putting a bee colony on the brink of collapse. For example, various members of the *Iflaviridae* family of viruses have been responsible for causing diseases that are characterized by severe damages and deformities to bee appendages. These bees are thus paralyzed at their legs and wings, and are no longer kept in the hive as they are unable to forage. In other cases, parasites, such as the microsporidian *Nosema ceranae*, are known to cause diseases by invading the intestinal lining of the bee gut; whereas the parasitic mite, *Varroa destructor*, is known to feed on the body of honeybees while spreading viral diseases (Dainat, Evans, Chen, Gauthier, & Neumann, 2012). At the same time, there has been links of CCD to pesticide use, especially with the pesticide class of neonicotinoids. All of these factors have been linked to CCD in one way or another, but there is no single identified cause. Identifying a single cause has proved challenging as the risk factors most likely vary on a case-by-case basis; indeed, interactions between the factors have also been described (Alaux, Brunet, & Dussaubat, 2010; Pettis, Johnson, & Dively, 2012). Therefore, CCD is most likely a combination of all these factors listed above.



The Easy Culprit: Pesticides.

Despite the uncertainty, the media has portrayed the use of pesticides as the sole contributor of CCD. The focus has been on modern-day neonicotinoids, which are globally used in insecticides to control agricultural insect pest. Compared to previous and older pesticides, such as organophosphates - the nerve agents also used in chemical warfare, neonicotinoids are much less harmful to humans, as they specifically target insect cells and not mammalian cells. In addition to the relatively low risk they pose to mammals and the environment, their versatility in application methods has moved neonicotinoids to the forefront of industry (Jeschke, 2008).

Without a doubt, neonicotinoids are toxic to bees. But are these pesticides really to be blamed for CCD? There has been debates of whether neonicotinoids are the sole contributor to CCD. Neonicotinoids are often applied on the coats of seeds, thereby limiting the contact point for bees to be exposed to this insecticide (Rondeau, 2014). However, trace amounts still persist in the pollen and nectar when these plants bloom. These trace amounts are ingested over a long period of time and can still have detrimental health consequences for bees, thereby affecting their ability to integrate sensory information from their environment (Dechaume Moncharmont, 2003). Imidacloprid, a widely-used neonicotinoid, is a neurotoxin that acts by binding irreversibly to

acetylcholine receptors in the CNS (Rondeau, 2014), thereby leading to paralysis and death for insects. Despite evidence of toxicity, there are questions regarding the validity of the forced-dose experiments in the real-world environment where neonicotinoids are metabolized. Studies that have examined the toxicity of neonicotinoids in treated crops, such as maize (corn) and oilseed rape, saw no disruption to the health of honeybee colonies due to neonicotinoids exposure versus untreated crops. However, in another experiment, exposures to neonicotinoids were only detrimental to bumblebees and wild bees (Eisenstein, 2015). The toxicity of neonicotinoids seems to be dependent on a case by case basis, which is often dependent on crop variety and application methods of neonicotinoids. For example, air-borne seed dust created by machines during the planting season has been responsible for the death of honeybees. However, improvement made to minimize the creation of seed dust have dramatically decreased the death of honeybees during the planting season (Eisenstein, 2015). UK's Crop Protection Association stated that a ban falling over modern pesticides including the neonicotinoid pesticide class, their farmers are forced to resort back to older more toxic, harmful and less effective pesticides. It should be noted that once the ban was placed in Europe in 2013, farmers did resort back to more harmful and less effective pesticides possibly causing more harm than benefit..

Despite the controversies surrounding pesticides including organochlorines, organophosphates and neonicotinoids, they are essential for modern agriculture and survival of a large portion of the world's population. Without crop protection products such as pesticides, the area required to grow the same amount of food would likely double (CropLife America, n.d.). The impact of pesticides follows a similar trend across all crops, with human population doubling in the past 50 years but the land used for agriculture remaining roughly constant. Furthermore, unlike the past, pesticides go through rigorous screening and safety testing by the EPA under the Federal Insecticide, Rodenticide, and Fungicide Act with over 120 toxicology and environmental tests to ensure the products do not pose a significant risk to the environment and the mammalian population (CropLife America, n.d.). That being said, it can cost up to \$256 million USD to develop and register a new usable product, with only 1 in 139,000 chemicals advancing to actual field use (CropLife America, n.d.).



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Today's agriculture competes with 30,000 different species of weeds (50-300 million seeds per acre), 3,000 species of nematodes, and some 10,000 species of plant-eating insects - all of which pesticides help discourage. Despite the use of pesticides, 20-40% of potential world food crop is still lost every year, a number which would be much higher without the intervention of crop protection products (Synegeta UK, 2013). Even organic farmers have their own class of non-synthetic pesticides - they typically use sulfur and copper to protect their crops from pests, though these are less effective pest managers.

Over the next 20-30 years, the United Nations has predicted the earth's population to rise by about 1.7 billion people, and with roughly 795 million people currently undernourished (Unknown, 2015), the human population needs a variety of resources to protect their crops while

increasing crop productivity. So the question remains: could we really do without pesticides, which we have used throughout our history of cultivation?

Governmental Policy Considerations of Neonicotinoids

In Canada, there is no ban on the use of neonicotinoids. The British Columbia Ministry of Agriculture, however, has tight regulations over the application of neonicotinoids, including bans on air application, application on crops with 15 metres of any aquatic system, and any use when wind speeds exceed 12-15 kilometres per hour or within 48 hours of rainfall. The Ontario Ministry of Agriculture recently introduced new pesticide legislation in July 2015, under which imidacloprid is considered a class 12 pesticide. As such, it may only be used under conditions of a demonstrated pest problem, in addition to written declarations of use, training for all stakeholders, and regular soil and crop inspections. Health Canada is in the process of establishing long-term regulations for neonicotinoid use, focusing primarily on stewardship practices. In addition, Health Canada has emphasized the need for government to collaborate with pesticide companies in order to effectively incorporate the latest technical improvements into regulation.

In the US, the neonicotinoid discussion has recently gained traction following a 2014 Presidential Memorandum on a federal strategy to promote honeybee health (Obama, 2014). The Environmental Protection Agency is currently in the process of reviewing neonicotinoid regulations, and is expected to conclude in 2018. Preliminary reports from the EPA suggest that neonicotinoid treatment of soybeans shows little to no benefit to overall crop yield.

In Europe, the Food Safety Agency found that neonicotinoids pose “high acute risks” to bees; as such, the European Union enforced a 2-year ban on neonicotinoids in 2013 and is currently set to be reviewed at the end of 2015. However, UK’s Department for Environment, Food and Rural Affairs (DEFRA) recently accepted an application by the National Farmers Union (NFU) allowing for the use of two neonicotinoid pesticides on 5% of England’s oilseed rape crop (Cressey, 2015). Believed to be due to infestations of the cabbage stem flea beetle, however the information provided by the NFU has not been made available to the general public citing the information being commercially sensitive.



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Economic Considerations of Pesticide Use

In British Columbia, the sale of bee products (honey, wax, and pollen) comprise \$10 million per year (BC Ministry of Agriculture). This has been steadily increasing for the past decade or so, with bee products only making up \$5.8 million in 2007. It has been estimated that bees contribute \$15 billion USD annually to the US economy through both bee products and the products of pollination. In Europe, bees have been estimated to contribute \$29 billion USD annually (Yale School of Forestry and Environmental Studies).

Neonicotinoids are used on 95% of corn and canola crops in the US, as well as the majority of cotton, fruit, vegetable, and soybean crops (Yale School of Forestry and Environmental

Sciences). Therefore, neonicotinoids comprise a significant proportion of the pesticide market. In 2008, imidacloprid accounted for 24% of the \$7.06 billion USD global pesticide market; for the insecticidal seed treatment market, which accounts for approximately \$1 billion USD of the pesticide market, imidacloprid makes up 80% (Bayer CropScience AG). Given the importance of neonicotinoids on crop protection and productivity, the cost of failed crops due to the European Commission ban on all neonicotinoid use in 2013, has been estimated to be between USD\$19-25 billion over a five year period (Eisenstein, 2015). However, the negative economic impact of neonicotinoid bans have not been well described. The Italian Ministry of Agriculture has reported that maize yield has not significantly changed since the government's introduction of an imidacloprid ban in 2008. Yet, in regions such as England and Scotland, oilseed rape seedlings have been hit hard with flea beetles (Eisenstein, 2015). Therefore, the negative economic impact from neonicotinoid bans will be dependent on the type of crops grown in different regions and the degree of which crop protection is needed.

Environmental Considerations of the impact of CCD

Beyond producing honey, bees play a crucial role in crop pollination which drives biodiversity of plants on this planet. Without bees, this planet will have to adapt to a future of decreased biodiversity in pollinated plants. According to the US Department of Agriculture, there has been on average a 30% decline in managed bee colonies each winter since 2006. This loss,



though, has much wider implications due to the keystone role of honeybees within the environment. The United States National Research Council (NRC-NAS) estimates that 75% of all flowering plant species rely on animal-based pollinators for reproduction (Berenbaum et al., 2006). Though *Apis mellifera* is by no means the only pollinator it is widely considered to be the most efficient (NRC-NAS, 2006), as evidenced by the fact that *A. mellifera* has remained the most important pollinator of crop monocultures worldwide since the mid-70s (McGregor, 1976; Vanengelsdorp & Meixner, 2010). In their review of 115 the leading global food crops, Klein et al.

(2007) found that 87 were reliant on animal-based pollination of which 52 relied heavily on honeybees. Furthermore, they found that five crops would have a >90% reduction in overall yield without honeybees, and sixteen would have a severe (40-90%) reduction in crop size or quality (Klein, Vaissiere, & Cane, 2007). Already, areas in mainland China are starting to see the use of people individually pollinating crops as minimal honeybee numbers are seen (Goulson, 2012). Therefore, can we really live without bees?

Can pesticides still be part of our future?

Based on aforementioned issues that arose from this report, imidacloprid is important to the protection of our crops from insect pest, while remaining selectively non-toxic to humans. Yet, we need to somehow, take into account of protecting the health of honeybees as they are crucial in pollinating our crops as well. Therefore, the 2015 UBC iGEM team proposed the use of a genetically engineered bee gut microbe to increase the non-toxic specificity of imidacloprid that grants protection of this pesticide to bees by detoxifying the neonicotinoid imidacloprid. Increasing the specificity of the pesticide is beneficial to all parties involved: crops stay protected from pests by imidacloprid, while bees avoid being caught in its collateral damage.

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